

AMENDMENTS TO THE SPECIFICATION

Please amend the specification as shown:

Please delete the paragraphs from page 39, line 15 to page 41, line 29 and replace them with the following paragraphs:

[0032] Figure 8 shows the sequence and predicted native conformation of fluorescent probe FP1. The FP1 sequence (SEQ ID NO: 21) comprises bases which are designed to be complementary to the target sequence and additional flanking bases. The flanking bases are underlined. Panel A (SEQ ID NO: 2) shows the predicted structure of the sequence using DNA folding programs according to *Nucleic Acids Res.* 31: 3429-3431 (2003). Panel B (SEQ ID NO: 2) shows predicted self dimerization of the FP1 sequence according to the oligoanalyzer 3.0 software available at <http://biotools.idtdna.com/analyzer/oligocalc.asp>. In both Panels A and B, the flanking bases are shaded in grey, white and black ovals indicate fluorophore and quencher moieties, respectively.

[0033] Figure 9 shows the sequence and predicted native conformation of fluorescent probe FP2 (SEQ ID NO: 23). The sequence comprises bases which are designed to be complementary to the target sequence and additional flanking bases. The flanking bases are underlined. Panel A (SEQ ID NO: 22) shows the predicted structure of the sequence using DNA folding programs according to *Nucleic Acids Res.* 31: 3429-3431 (2003). It is likely that all or part of the shaded region form Watson-Crick basepairs, thereby forming a three-arm junction. Panel B (SEQ ID NO: 22) shows predicted self dimerization of the FP2 sequence according to the oligoanalyzer 3.0 software available at <http://biotools.idtdna.com/analyzer/oligocalc.asp>. In both Panels A and B, the flanking bases are shaded in grey, white and black ovals indicate fluorophore and quencher moieties, respectively.

[0034] Figure 10 shows the sequence and predicted native conformation of fluorescent probe FP3. The FP3 sequence (SEQ ID NO: 25) comprises bases which are designed to be complementary to the target sequence and additional flanking bases. The flanking bases are underlined. The figure (SEQ ID NO: 24) shows predicted self dimerization of the FP3 sequence according to the oligoanalyzer 3.0 software available at <http://biotools.idtdna.com/analyzer/oligocalc.asp>. The flanking bases are shaded in grey, white and black ovals indicate fluorophore and quencher moieties, respectively.

[0035] Figure 11 shows the sequence and predicted native conformation of fluorescent probe FP4 (SEQ ID NO: 26). The FP4 sequence comprises bases which are designed to be complementary to the target sequence and additional flanking bases. The flanking bases are underlined. The figure (SEQ ID NO: 24) shows the predicted structure of the sequence using DNA folding programs according to *Nucleic Acids Res.* 31: 3429-3431 (2003). The flanking bases are shaded in grey, white and black ovals indicate fluorophore and quencher moieties, respectively.

[0036] Figures 12 through 13 show the sequences of fluorescent probes FP5 (SEQ ID NO: 27) to FP6 (SEQ ID NO: 28). The sequences comprises bases which are designed to be complementary to the target sequence and additional flanking bases. The flanking bases are underlined.

[0037] Figure 14 shows the sequence and predicted native conformation of fluorescent probe FP7 (SEQ ID NO: 29). The FP7 sequence comprises bases which are designed to be complementary to the target sequence and additional flanking bases. The flanking bases are underlined. The predicted self dimerization of the FP7 sequence according to the oligoanalyzer 3.0 software available at <http://biotools.idtdna.com/analyzer/oligocalc.asp> is shown. The flanking bases are shaded in grey, white and black ovals indicate fluorophore and quencher moieties, respectively (SEQ ID NO: 24).

[0038] Figure 15 shows the sequence and predicted native conformation of fluorescent probe FP8 (SEQ ID NO: 32). The FP8 sequence comprises bases which are designed to be complementary to the target sequence and additional flanking bases. The flanking bases are underlined. Panel A (SEQ ID NO: 30) shows the predicted structure of the sequence using DNA folding programs according to *Nucleic Acids Res.* 31: 3429-3431 (2003). Panel B (SEQ ID NO: 31) shows predicted self dimerization of the FP1 sequence according to the oligoanalyzer 3.0 software available at <http://biotools.idtdna.com/analyzer/oligocalc.asp>. In both Panels A and B, the flanking bases are shaded in grey, white and black ovals indicate fluorophore and quencher moieties, respectively.

[0039] Figures 16 through 20 show the sequences of fluorescent probes FP9 to FP13 (SEQ ID NOS: 33-37, respectively). The sequences comprises bases which are designed to be complementary to the target sequence and additional flanking bases. The flanking bases are underlined.

[0040] Figure 21 shows the sequence and predicted native conformation of fluorescent probe FP14 (SEQ ID NO: 39). The FP14 sequence comprises bases which are designed to be complementary to the target sequence and additional flanking bases. The flanking bases are underlined. The figure (SEQ ID NO: 38) shows the predicted structure of the sequence using DNA folding programs according to *Nucleic Acids Res.* 31: 3429-3431 (2003). The flanking bases are shaded in grey, white and black ovals indicate fluorophore and quencher moieties, respectively.

[0041] Figures 22 through 24 show the sequence and predicted native conformation of fluorescent probes FP15 to 17 (SEQ ID NOS: 41, 43 and 45, respectively), respectively. The sequences comprises bases which are designed to be complementary to the target sequence and additional flanking bases. The flanking bases are underlined. Panel A shows the predicted structure of the sequence using DNA folding programs according to *Nucleic Acids Res.* 31: 3429-3431 (2003). Panel B shows predicted self dimerization of the FP15 sequence according to the oligoanalyzer 3.0 software available at <http://biotools.idtdna.com/analyzer/oligocalc.asp>. In both Panels A and B, the flanking bases are shaded in grey, white and black ovals indicate fluorophore and quencher moieties, respectively. (Figure 22: Panels A and B disclose SEQ ID NO: 40. Figure 23: Panels A and B disclose SEQ ID NO: 42. Figure 24: Panels A and B disclose SEQ ID NO: 44).

Please delete the paragraph on page 44, lines 1-9 and replace it with the following paragraph:

[0049] Figure 32 shows fluorescence images of drug selected HeLa cells transfected with an expression plasmid encoding a portion of the sequence of vav cloned in reverse orientation (referred to r-vav) as well as a drug resistance gene. The cells were exposed to fluorescent probes (FP) designed to recognize the same target sequence within r-vav (5' GTTCTTAAGGCACAGGAAGTGGGA 3') (SEQ ID NO: 1). The images were obtained using a fluorescence microscope and filters designed to detect fluorescence from Fam. All FPs used here were labeled using FAM except FP1, which was labeled using fluorescein. Panel A, B, C, D each were exposed to FP10, FP11, FP12 and FP13.

Please delete the paragraphs from page 44, line 23 to page 46, line 2 and replace them with the following paragraphs:

[0052] Figure 35A (SEQ ID NO: 46) shows a portion of (underlined) the reverse complement of the vav DNA sequence (r-vav DNA) selected for forming the tag sequence. This sequence was cloned into an expression plasmid designed to express r-vav mRNA. The sequence indicated in bold is the target sequence for certain fluorescent probes. Figure 35B (SEQ ID NO: 47) shows the sequences underlined in Figure 35A after they have been combined to form a tag sequence (tag1 sequence).

[0053] Figure 36A (SEQ ID NOS: 69-71) shows the predicted structure of part of the r-vav RNA using RNA folding programs in *Nucleic Acids Res.* 31: 3429-3431 (2003). Figure 36B (SEQ ID NO: 68) is the predicted structure of the tag1 sequence shown in Figure 35B. The shading indicates the target sequence designed to be recognized by some of the fluorescent probes.

[0054] Figures 37A (SEQ ID NO: 65), B (SEQ ID NO: 66) and C (SEQ ID NO: 67) show the predicted structures for tag 1, 2 and 3 sequence as described in Figure 42. These structures resemble each other but present a different sequence for recognition by fluorescent probes. The prediction was generated using RNA folding programs in *Nucleic Acids Res.* 31: 3429-3431 (2003).

[0055] Figure 38 shows fluorescence signal emitted from FPs in solution in the presence of target or control oligo sequence. Samples were illuminated by UV and photographed. All FPs used here incorporated Fluorescein. Tubes each contained 16ul total consisting of 5ul of a 20uM FP stock, 1.5ul 25mM MgCl₂, 8ul 20uM oligo, and 1.5ul of water, having a final magnesium concentration of approximately 2.34 mM. FP1 and FP18 were used here and were synthesized incorporating sulfur linkages between the bases of the sequence designed to recognize target oligos TO-FP1 and TO-FP18, respectively. FP1 is directed against the sequence of target oligo 1 (TO-FP1 5'GTTCTTAAGGCACAGGAAGTGGGA3') (SEQ ID NO: 1), and FP 18 is directed against the sequence of target oligo FP18 (TO-FP18 5'TCCCAGTTCCTGTGCCTTAAGAAC3') (SEQ ID NO: 2). The sequences of TO-FP1 and TO-FP18 were reverse complements of each other. TO-FP18 has sequence not targeted by FP1

and served as a control oligo for FP1. TO-FP1 has sequence not targeted by FP18 and served as a control oligo for FP18.

In all Panels, the compositions of the tubes are as indicated below:

tube	FP	oligo
1	FP18	TO-FP18
2	FP18	TO-FP1
3	FP1	TO-FP18
4	FP1	TO-FP1

This figure shows that each of the FPs tested were specifically reporting the presence of target sequences by emitting a greater signal in tubes containing oligos having targeted sequence as compared to control tubes containing oligos having non-targeted sequence. Tubes containing FPs in the presence of oligos comprising target sequence are indicated by asterisk.

Please delete the paragraph from page 46, line 22 to page 47, line 6 and replace it with the following paragraph:

[0059] Sequences from 5' to 3' direction for TO-M1, TO-M2 and TO-M3 are listed below:

TO-M1:

TTTCTCTGTGATCCGGTACAGTCCTTCTGCGCAGGTGGACAGGAA
GGTTCTAATGTTCTTAAGGCACAGGAAGTGGGACATCTGGGCCCCG
GAAAGCCTTTTTCTCTGTGATCCGGTACAGTCCTTCTGCGCAGGT
GGACAGGAAGGTTCTAATGTTCTT (SEQ ID NO: 3)

TO-M2:

TTTAACTGATGGATGGAACAGTCCTTCTGCGCAGGTGGACAGCTT
GGTTCTAATGAAGTTAACCCTGTCGTTCTGCGACATCTGGGCCCCG
GAAAGCGTTTAACTGATGGATGGAACAGTCCTTCTGCGCAGGTGG
ACAGCTTGGTTCTAATGAAGTT (SEQ ID NO: 4)

TO-M3:

GTAAAGTCAGACATCCGGTACAGTCCTTCTGCGCAGGTGGACAGG
AAGGTTCTAATGTTCTATAGGGTCTGCTTGTCGCTCATCTGGGCC
CGGAGATGCGTAAAGTCAGACATCCGGTACAGTCCTTCTGCGCAG
GTGGACAGGAAGGTTCTAATGTTCTAT (SEQ ID NO: 5)

Please delete the paragraphs from page 47, line 20 to page 48, line 9 and replace them with the following paragraphs:

[0062] Figure 41 shows the sequence and predicted native conformation of fluorescent probe FP18 (SEQ ID NO: 48). The sequence comprises bases which are designed to be complementary to the target sequence and additional flanking bases. The flanking bases are underlined. Panel A (SEQ ID NO: 1) shows the predicted structure of the sequence using DNA folding programs according to *Nucleic Acids Res.* 31: 3429-3431 (2003). Panel B (SEQ ID NO: 1) shows predicted self dimerization of the FP2 sequence according to the oligoanalyzer 3.0 software available at <http://biotools.idtdna.com/analyzer/oligocalc.asp>. In both Panels A and B, the flanking bases are shaded in grey, white and black ovals indicate fluorophore and quencher moieties, respectively.

[0063] Figures 42A (SEQ ID NO: 49), B (SEQ ID NO: 50) and C (SEQ ID NO: 51) show the three tag sequences recognized by fluorescent probes. In Figures 42A, B and C, the target sequences (SEQ ID NOS: 1, 52 and 53, respectively) are indicated in bold and they are also shown in Figure 42D. The first sequence (tag1, 42A) is the same as the sequence indicated in Figure 35B. The next two sequences (tag2, 42B and tag3, 42C) are altered versions of tag1. The differences in sequence of target2 and target3 as compared to target1 is underlined in Panel D. Additional sequence changes were made in the remaining tag sequences to compensate for the changes made in the portions shown.

[0064] Figure 43 shows the design of tag2 sequence from tag1 sequence. A-F (SEQ ID NOS: 54-59, respectively) indicate the sequential base changes made during the design.

[0065] Figure 44 shows the design of tag3 sequence from tag1 sequence. A-[[F]]G (SEQ ID NOS: 54, 60-64 and 9, respectively) indicate the sequential base changes made during the design.

Please delete the paragraph on page 105, lines 12-21 and replace it with the following paragraph:

[0260] Fifteen different chemically modified probes based on the FP1 probe sequence were synthesized. All of these probes have the same sequence and are directed against the same target sequence. The probes were introduced into 293T cells. These cells express a tag sequence that includes the target sequence of FP1. FACS was used to analyze the fluorescence from these cells. The fifteen different probes are described below (SEQ ID NOS: 6-8, 2 and 10-20 are disclosed respectively in order of appearance). The results of the FACS analysis are shown in Figs. 46-60. The results show that all fifteen of the probes are able to detect cells expressing the target sequence. All of the probes were identical with respect to concentration, method of delivery, fluorophore, quencher and sequence except for the chemical modification.

Please insert a copy of the Sequence Listing submitted herewith (pages 1-25) at the end of the specification, after the Abstract.